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HARNESS, DICKEY & PIERCE, P.L.C.
P.O.BOX 8910
RESTON, VA 20195

EXAMINER	
WANG, CHANG YU	

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1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,702	OLAUSSON ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-112* is/are pending in the application.

4a) Of the above claim(s) *104-112* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/29/05,1/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION
Status of Application/Election/Restrictions

1. Applicant's election with traverse of Group I (claims 57-103) in the reply filed on 10/14/2008 is acknowledged. The traversal is on the ground(s) that Groups I and II share a special technical feature because US Patent No. 6548569 (the '569 patent) teaches devices formed by a biodegradable polyhydroxyalkanoate polymer having degradation rates of less than one year in vivo wherein the degradation rate is manipulated through chemical or physical composition of the polymer. Applicant argues that the device of the '569 patent does not relate to the in vivo degradation of the devices to the tissue regeneration time or the time required for establishing regenerated contact between ends of an injured nerve. Applicant's arguments have been fully considered but they are not persuasive. In contrast, as previously made of record, the instant device and the device disclosed by the '569 patent comprise the same compositions (polyhydroxybutyrate, PHB) and structures (nerve guides made from polyhydroxybutyrate such as poly-4-hydroxybutyrate, poly-3-hydroxybutyrate in a form of sheet or channel) (see col.7, lines 31-49; col.16, lines 42-52). As long as the structures and compositions are identical, the prior art anticipates the claimed invention. In this case, the limitations recited in the wherein clause do not result in structural or functional difference from the prior art. Thus, if the instant device can promote increasing axon growth and regeneration as claimed, the prior art device would also have the same activity as claimed because the composition and structures of the claimed device are identical to those of the prior art (also see the rejection under

35USC 102(b)). Applicant fails to provide evidence to distinguish that the effects derived from the claimed device are resulted from different structures or compositions from those of the prior art. Thus, Group I has no special technical feature and thus cannot share a special technical feature with the other claimed inventions. Accordingly, Applicant's inventions do not have a single inventive concept and thus lack unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 57-112 are pending. Claims 104-112 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 57-103 are under examination in this office action.

Claim Objections

3. Claims 104-112 are objected to because of the following informalities: the status of the claims 104-112 is not correct because these claims are withdrawn from consideration. Appropriate correction is required.

See MPEP 714 & 37 CFR 1.121.
"In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered)."

4. Claims 57-103 are objected to because of the following informalities:

the recitations "t1, tc, t2, tr, PHB, PLGA" recited in the claims 57-61, 65-67, 69, 83-, 91-92,100-101 are not a common abbreviation in the art. Applicants are required to spell out "t1, tc, t2, tr, PHB, PLGA" at the first usage. Appropriate correction is required.

In addition, independent claim 57 should be rewritten as:

"a device/kit for promoting regeneration of an injured nerve, comprising:

a nerve encasement structure and

a plurality of biodegradable guiding units, wherein at least a majority of the guiding units present an in vivo degradation time (t1) being less than ~~a~~ the time ~~te~~ required for establishing regenerated contact between ends of an injured nerve (tc) using the device for said regeneration.

Independent claim 60 should be rewritten as:

"a device/kit for promoting regeneration of an injured nerve comprising:

a nerve encasement structure and

a plurality of biodegradable guiding units

wherein at least a majority of the guiding units present an in vivo degradation time (t1), wherein at least a major part of the nerve encasement structure presents an in vivo degradation time (t2), wherein t2 ~~being~~ is longer than t1 and is longer than the time ~~tr~~ required for the entire nerve regeneration process to be completed (tr), and wherein t1 ~~being~~ is less than tr.

The above revisions in claims 57 and 60 are applied to all of the subsequently claims, in particular claims 81-83, 100-101. Appropriate correction is required.

Furthermore, claims 69-70 and 91-92 recite a molecular weight of "50,000 to 500,000" or "100,000 to 250,000" or "50, 000to <250,000" without a unit. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57-103 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 57-103 are indefinite because the terms "t1, tc, t2, and tr" are recited in the claims without a reference to a precise time. Although the specification describes the meanings for the terms of t1, tc, t2 and tr on p.12-15 of the specification, it is unclear to the examiner or a skilled artisan what exact time units would be within the definition of these terms. Without identification of time units or combination of different features and times which are unique to and, therefore, definitive of the instant recitations, the metes and bounds of the claims remain undetermined. Further, the use of laboratory designations only to identify a particular term renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct terms. The rejection can be obviated by amending the claims to specifically and uniquely identify t1, tc, t2, and tr, for example, by a specific time or formula of t1, tc, t2, and tr.

In addition, claims 58-59, 61-80, 82, 84-99, 102 and 103 are indefinite because they recite "A device/kit/sheet according to claim x (the independent claim)". The article "A" connotes that there is more than a single product encompassed within the base claim and since only a single product was set forth therein, it is unclear what, if any, additional products are encompassed.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 57-103 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 57-103 are drawn to a device/kit/biodegradable sheet for promoting regeneration comprising a nerve encasement structure and a plurality of biodegradable guiding units. The guiding units disclosed in the claimed device/kit/biodegradable sheet have an in vivo degradation time (t1) that is less than tc, which is the required for establishing regenerated contact between ends of an injured nerve. The nerve encasement structure has an in vivo degradation time (t2) that is longer than t1. The t2 is also longer than tr, which is the time required for the entire nerve regeneration

process to be completed, and the t1 is less than tr. The claims encompass a genus of devices/kits/biodegradable sheets comprising a genus of guiding units with properties of t2 being longer than t1 and tc and t1 being less than tr.

The instant specification has not disclosed sufficient species for the broad genus of t1, tc, t2 and tr to make a genera of devices/kits/biodegradable sheets having the properties as claimed. The specification only describes nerve conduits are constructed from a nonwoven sheet of polyhyroxybutryate (PHB) having a molecular weight of 140,000, a sheet thickness of 0.25mm and a weight per unit area of 10mg/cm2. The described conduit was evaluated for their ability to cross a 1cm gap in the sciatic nerve of rats (see the example on p.26-27 of the specification). However, the claims are not limited to the conduit as set forth above.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant is in possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of a conduit made from a non-woven sheet of polyhyroxybutryate (PHB) having a molecular weight of 140,000, a sheet thickness of 0.25mm and a weight per unit area of 10mg/cm2 and filled with non-bonded PHB fibers with an average molecular weight of 80,000 and cross-sectional dimensions within the range of 5-15μm wherein the conduit is able to repair a 10mm gap of an injured sciatic nerve. Although the specification describes the meanings for the terms of t1, tc, t2 and tr on p. 12-15 of the specification, Applicant is not in possession all forms of device comprising undefined guiding units having the undefined

properties as set forth in independent claims. The specification fails to provide other common structures, compositions or features that are required for any conduit comprising any guiding units having the properties of t2 being longer than t1 and tc, and of t1 being less than tr. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features for the all of the devices comprising all of the guiding units and a nerve encasement structure/sheet/kit having the claimed genus of t1, tc, t2 and tr parameters. In addition, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to envision what t1, tc, t2 and tr might be. Since the common characteristics/features required for the claimed genera are unknown, a skilled artisan cannot envision the functional correlations of the genus with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of devices/kits/biodegradable sheets.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical and physical structure of the encompassed genera of devices/kits/biodegradable sheets, and therefore

conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the claimed devices/kits/biodegradable sheets have not met the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement. See MPEP § 2163.

7. Claims 57-103 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 57-103 recite limitation of "guiding units", which was not clearly disclosed in the specification and claims as originally filed, and now change the scope of the instant disclosure as filed. Such limitation recited in the present claims, which did not appear in the specification or original claims, as filed, introduces new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The specification fails to disclose the limitation "guiding units" as recited in instant claims 57-103. The specification only discloses "guiding means" across the specification). The specification provides no guidance as to what is encompassed in the "guiding units". Accordingly, in the absence of sufficient recitation of "guiding units", the specification does not provide adequate written description to support such limitation as recited in instant claims. Thus the recitation of "guiding units" constitutes new matter absent evidence for their support. Applicant is required to cancel the new matter in the reply to this office action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 57-67, 71-74, 77-89, 93-97, and 100-103 are rejected under 35 U.S.C. 102 (b) as being anticipated by US Patent No. 6548569 (Williams et al. issued

Apr 15, 2003, priority Mar 25, 1999.) as evidenced by US. Patent No. 5584885 (Seckel, issued on Dec 17, 1996) and Clavijo-Alvarez et al. (Plast. Reconstr. Surg. 2007. 119:1839-1851).

Claims 57-61, 82-83 and 100-101 are drawn to a device/kit/biodegradable sheet for promoting regeneration of an injured nerve, comprising: a nerve encasement structure/biodegradable sheet/an dehydrate hydrogel and a plurality of biodegradable guiding units, wherein at least a majority of the guiding units present "t1" being less than "tc" and "tr", and at least a major part of the nerve encasement structure/sheet/hydrogel presents "t2" being longer than "t1" and "tr", wherein "t1" is the in vivo degradation time of the guiding units, "t2" is the in vivo degradation time of the nerve encasement structure/sheet/hydrogel, "tc" is the time required for establishing regenerated contact between ends of an injured nerve and "tr" is the time required for the entire nerve regeneration process to be completed.

Dependent claims are directed to as follows: the guiding units are guiding fibers (claims 62, 84, 102), the materials of the guiding units and the nerve encasement are polymer (claims 63, 85), polyester (claims 64, 86), PHB (claims 65-66, 87-88) or PHB for the nerve encasement and PLGA for the guiding units (claims 67, 89). In addition, the nerve encasement structure comprises a compressed non-woven sheet with a unidirectional fiber orientation (claims 71, 93) and the guiding units comprise a non-bonded fiber web with a unidirectional fiber orientation (claims 72, 94). Furthermore, the device/kit/sheet further comprises a dehydrate hydrogel matrix (claims 73, 95-96), an active substance or cell (claims 74-77, 97-99 and 103). Moreover, the guiding units

occupy ≤2.0% by volume of the lumen formed by the nerve encasement structure (claim 77), the cross-section dimension of the guiding units is ≤50μm (claim 78), ≤20μm (claim 79), 5-15μm (claim 80).

US Patent No. 6548569 (the '569 patent) teaches a device for promoting regeneration of an injured nerve comprising a nerve encasement structure and a plurality of biodegradable guiding units as recited in instant claims 57-67, 71-74, 77-89, 93-97, and 100-103. The '569 patent teaches a biodegradable device comprising poly-4-hydroxybutyrate (PHB) (see col.7, lines 31-33, in particular) in a form of porous conduit such as having the shape of the nerve conduit products of NEUROTUBE™ as incorporated by the references including US Patent NOs. 5735863, 5584885 and 5026381. The device disclosed by the '569 patent meets the limitation of "the device comprising a nerve encasement structure and a plurality of biodegradable guiding units as recited in independent claims 57-61, 82-83 and 100-101 because the shape of the NEUROTUBE is a nerve encasement structure and the PHB polymers are fabricated into fibers, sheets, foams, coating structures, filaments, which are a plurality of biodegradable guiding units as recited in the independent claims (see col. 16, lines 42-52; co. 25, line 50-col. 28, lines 35, in particular). The device disclosed by the '569 patent is made from biocompatible polyhydroxyalkanoates (PHA) comprising poly-4-hydroxybutyrate (P4HB, which is one of PHB) polymers as recited in instant claims 63-66 and 85-88 because P4HB is a polymer, a polyester and a PHB (see col. 4, lines 20-57; col.7, lines 31-35, in particular). The '569 patent also teaches that poly-4-

hydroxybutyrate (P4HB, one of PHB) polymers can be fabricated into fibers, sheets, foams, coating structures, filaments for implantable medical materials, which meet the limitations of "the guiding units are guiding fibers" as recited in instant claims 62, 84, 102 (see col. 37-39, examples 6-11; col. 39, lines 41-46, in particular).

In addition, the orientation of P4HB the nerve encasement structure made of P4HB comprises a compressed non-woven sheet (i.e. non-bonded fiber web) with a unidirectional fiber orientation as recited in instant claims 71-72 and 93-94 (see col. 37-39, examples 8-11, in particular). The device also encompassed cells or other active agents as recited in instant claims 74-77, 97-99 and 103 (see col. 25, line 50- col. 27, line 35; col. 37, example 7, in particular). In addition, the device can also made by the methods disclosed by US Patent No. 5584885 (i.e. one of the incorporated references in the '569 patent). The '885 patent teaches nerve guides (i.e. nerve conduits) comprising Schwann cells, growth factors and drugs as recited in instant claim 75-76 and 98-99 (see col.7, lines18-col.8, lines 29; col. 16, lines 22-60, in particular).

Further, the device/kit/sheet disclosed by the '569 patent also comprises PLGA as in instant claims 67, 89 and a dehydrate hydrogel matrix as in instant claims 73, 95-96 because the '569 patent teaches sheets made from PHB and PGA (which is the same as PLGA) (see col. 38-39, examples 10-11, in particular) and also teaches patches including silicone membranes, polyurethane, fascia, lata, Gore-Tex etc, which meets the limitation of "a dehydrate hydrogel matrix" and PHB foams coating of a PGA non-woven mesh (see col. 16, line 63- col.17, line 7; col. 25, line 50- col. 27, line 35; col. 39, example 11, in particular). Furthermore, The '569 patent also teaches formation of

PHB microspheres with the size of 1-10μm(see col. 39, example 12, in particular), which meet the limitation of " the cross-section dimension of the guiding units is ≤50μm, ≤20μm or 5-15μm as recited in instant claims 78-80.

Moreover, since neither the specification nor the claims specify the dimension of the claimed device, the claimed nerve encasement or the definition of the guiding units, the teachings of the '569 patent meets the limitations of "the guiding units occupy ≤2.0% by volume of the lumen formed by the nerve encasement structure (claim 77

The specification only describes a conduit made from a non-woven sheet of polyhyroxybutryate (PHB) having a molecular weight of 140,000, a sheet thickness of 0.25mm and a weight per unit area of 10mg/cm2 and filled with non-bonded PHB fibers with an average molecular weight of 80,000 and cross-sectional dimensions within the range of 5-15μm wherein the conduit is able to repair a 10mm gap of an injured sciatic nerve. Since the structures and compositions of the nerve guides or devices disclosed by the '569 patent are the same as those described in the specification, the prior art would also have the same properties of t1, t2, tc and tr as recited in instant claims. Thus, claims 57-67, 71-74, 77-89, 93-97, and 100-103 are anticipated by US Patent No. 6548569.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 57-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6548569 (Williams et al., issued on Apr 15, 2003, priority date Mar 25, 1999) in view of US Patent No. 5656605 (Hansson et al., issued Aug 12, 1997) and US. Patent No. 5584885 (Seckel, issued on Dec 17, 1996).

Claims 57-61, 82-83 and 100-101 are drawn to a device/kit/biodegradable sheet for promoting regeneration of an injured nerve, comprising: a nerve encasement structure/biodegradable sheet/an dehydrate hydrogel and a plurality of biodegradable

guiding units, wherein at least a majority of the guiding units present "t1" being less than "tc" and "tr", and at least a major part of the nerve encasement structure/sheet/hydrogel presents "t2" being longer than "t1" and "tr", wherein "t1" is the in vivo degradation time of the guiding units, "t2" is the in vivo degradation time of the nerve encasement structure/sheet/hydrogel, "tc" is the time required for establishing regenerated contact between ends of an injured nerve and "tr" is the time required for the entire nerve regeneration process to be completed.

Dependent claims are directed to as follows: the guiding units are guiding fibers (claims 62, 84, 102), the materials of the guiding units and the nerve encasement are polymer (claims 63, 85), polyester (claims 64, 86), PHB (claims 65-66, 87-88) or PHB for the nerve encasement and PLGA for the guiding units (claims 67, 89). The molecular weight of the guiding units are less than that of the encasement (claims 68, 90); for example, the molecular weight of PHB is 50,000-500,000 Daltons (claims 69,91) or 100,000-250,000 Daltons for the nerve encasement and 50,000 to <250,000 for the guiding unit (claims 70, 92). Further, the nerve encasement structure comprises a compressed non-woven sheet with a unidirectional fiber orientation (claims 71, 93) and the guiding units comprise a non-bonded fiber web with a unidirectional fiber orientation (claims 72, 94). Furthermore, the device/kit/sheet further comprises a dehydrate hydrogel matrix (claims 73, 95-96), an active substance or cell (claims 74-77, 97-99 and 103). Moreover, the guiding units occupy $\leq$2.0% by volume of the lumen formed by the nerve encasement structure (claim 77), the cross-section dimension of the guiding units is $\leq$50μm (claim 78), $\leq$20μm (claim 79), 5-15μm (claim 80).

US Patent No. 6548569 is as set forth above but does not teach an active substance and cells as recited in instant claims 75-76 and 98-99. The '569 patent also does not explicitly teach that the molecular weight of the guiding units is less than that of the encasement (claims 68, 90); for example, the molecular weight of PHB is 50,000-500,000 Daltons (claims 69,91) or 100,000-250,000 Daltons for the nerve encasement and is 50,000 to <250,000 for the guiding unit (claims 70, 92).

US Patent No. 5584885 (i.e. one of the incorporated references in the '569 patent) teaches nerve guides (i.e. nerve conduits) comprising Schwann cells, growth factors and drugs as recited in instant claim 75-76 and 98-99 (see col.7, lines18-col.8, lines 29; col. 16, lines 22-60, in particular).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to incorporate Schwann cells, other cells or growth factors for nerve regeneration. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because the '885 patent has shown to generate a nerve guide containing Schwann cells, other cells or growth factors as recited to promote nerve regeneration.

In addition, although the '569 patent does not explicitly teach that the molecular weight of PHB is 50,000-500,000 Daltons or 100,000-250,000 Daltons for nerve encasement and the molecular weight of PHB is 50, 000-less than 250,000Daltons, the '569 patent teaches that the units of PHB polymers are 10-100,000 and preferably 100-30,000units and that the molecular weight of the PHB polymers for biodegradable

devices is between 10,000-10,000,000Dalton (see col. 5, lines 40-col. 6, line 10; col. 39, claim 1, in particular). The '569 patent also teaches that the device comprising PHB polymers can be coated or fabricated to medical device to improve their compatibility, tailoring their degradation and controlled release profiles (see col. 27, lines 1-35, in particular).

US Patent No. 5656605 teaches nerve guides for promoting nerve regeneration comprising a guide tube, guiding filaments and a therapeutic composition enclosed by the guide tube wherein both the nerve guide and the nerve filaments are composed of a nerve-growth stimulating agent in a matrix-forming material (see abstract). The '605 patent also teaches that the nerve guide tube is made of biological inert polymer such as polyglycolic acid (PGLA) and therapeutic composition such as methylcellulose gel and a nerve-growth stimulating agents such as IGF-like, NGF, PDGF and Schwann cells (see col. 2, lines 41-col. 3, line 24; col.2, line 42-col.5, line 7, in particular). The inert polymeric material includes collagen complexes, polylactic acid, polyglycolic acid, polyetraethyelen, silastic, poly-n-aceylglucosamine or polymer into which growth factors can be incorporated directly for the nerve guide tubes. The nerve guide thread filaments can be the same as the nerve guide tube or other compatible substances for formation of a cable of axon regeneration and the materials for carrier matrices include collagen, methylcelluose gel, fibrin other blood derived proteins, extracellular matrix such as Matrigel, Biomatrix and nerve-growth stimulating agents include Insulin like growth factors, FGF, a/bFGF, TGF, PDGF, BDGF, CNTF etc. and the cells include Schwann

cells, endothelial cells, fibroblasts (see col.3, lines 5-24; col. 3, line 52-col.5, line 7, in particular).

It would also have been obvious to one of ordinary skill in the art at the time the instant invention was made to make a device having a nerve encasement structure and guiding units wherein the molecular weight of guiding units is less than that of the encasement to optimize different molecular weights of PHB for the nerve encasement and guiding units to tailor the in vivo degradation time and compatibility of the device for nerve regeneration purposes. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because the '569 patent teaches that PHB polymers with different molecular weights would degrade differently and the PHB polymers with a molecular weight between 10,000-10,000,000Dalton are expected to work for repair or regeneration and the '605 patent teaches a device encompasses a guide tube, guiding filaments and a therapeutic composition enclosed by the guide tube.

Note that

In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie*case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990), See MPEP 2144.05-I.

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105USPQ 233, 235 (CCPA 1955)" See MPEP 2144.05-II.

Conclusion

10. NO CLAIM IS ALLOWED.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US Patent No. 5358475 (as in IDS) teaches nerve channels made from poly-lactic acid polymers having a molecular weight between 234000-32000 for nerve regeneration.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
January 8, 2008

/Christine J Saoud/
Primary Examiner, Art Unit 1647